UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,752	03/31/2004	Paul L. DeAngelis	4599.014	8611

30589 7590 12/27/2007
DUNLAP CODDING & ROGERS, P.C.
PO BOX 16370
OKLAHOMA CITY, OK 73113

EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
12/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,752	DEANGELIS, PAUL L.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed October 16, 2007 amending claim 8, canceling claims 14-18 and adding claims 19-23 has been entered.

Claims 8 and 19-23 are pending.

Election/Restrictions

Applicant's election of Group I, claim 8, in the reply filed on October 16, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 19-23 are rejoined with claim 8.

Information Disclosure Statement

Reference AX on the information disclosure statement filed November 30, 2004 was not provided and therefore, was not considered.

Specification

The specification is objected to because it does not comply with the Sequence Rules. 37 CFR 1.821(c) requires that each sequence that appear in the specification being assigned a sequence identification number, i.e. SEQ ID NO. However, in the instant specification the same sequence is being assigned two SEQ ID NOs. For

example, SEQ ID NO: 2 (617 amino acids) is 100% identical to SEQ ID NO: 4 (617 amino acids).

The specification is objected to because it recites GenBank accession "AF438904" (e.g., page 14, [0038]) wherein the correct number is "AF439804"

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 has been amended and claims 19-23 have been added on October 16, 2007 to recite "a soluble heparin synthase having an amino acid sequence that is at least 70% identical to at least one of SEQ ID NO: 13 or 15". While there is support in the specification for sequences that are 70% identical to SEQ ID NOs: 12 or 14 (page 23, [0055]), i.e. to the nucleic acid sequences, the examiner is unable to locate adequate support in the specification for sequences that are 70% identical to SEQ ID NOs: 13 or 15, i.e. to the amino acid sequences. Thus there is no indication that soluble heparin synthases having the amino acid sequences that are at least about 70% identical SEQ

ID NOs: 13 or 15 were within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

Claims 8 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 and claim 19, with dependent claims 20-23, recite in "(F)" "a soluble heparin synthase having an amino acid sequence that is a fragment of at least one of SEQ ID NOS: 2, 4, 13 and 15". Since the fragment can be of any size and is not limited to having heparin synthase activity, the claims encompass the genus of heparin synthases both naturally occurring and man made having any structure and properties defined by enzymatic function only.

In the instant specification the diverse and variable genus of heparin synthases is represented by heparin synthase (pmHS1) from *Pasteurella multocida* having the amino acid sequence of SEQ ID NO:2 (100% identical to SEQ ID NO:4) and its truncated soluble versions having SEQ ID NOs: 13 and 15 (page 14, [0037]). The specification fails to describe any other representative species from any source by any identifying

characteristics or properties other than the functionality of being heparin synthase and does not disclose the structure: function correlation common to all members of the genus. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 8 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a heparin polymer from UDP-GlcNAc and UDP-GlcUA using heparin synthase of SEQ ID NOs:2, 13 or 15 in the presence of divalent ion and a method elongating the acceptor using the same, does not reasonably provide enablement for methods of use of heparin synthase having an amino acid sequence with no known identity to SEQ ID NOs: 2, 13 or 15 or having at least 70% identity to SEQ ID NOs: 13 or 15 or encoded by a DNA that hybridizes to SEQ ID NOs: 12 or 14 under hybridization conditions recited in clause "(D)" of claims 8 and 19 as well as for a method for elongating the acceptor without a divalent ion. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The prior art teaches a nucleic fragment from *Pasteurella multocida* of 7569 bp, nucleotides 2891-4743 of which are 99.1% identical to SEQ ID NO:1 of the instant invention. It encodes a protein of 501 amino acids. SEQ ID NO:2 of the instant invention is 79.7% identical thereto with residues 1-497 of SEQ ID NO:2 being 99.4% identical to residues 1-497 of the amino acid sequence (Townsend et al., J. Clin. Microbiology, March 2001, 39 (3), 924-929, form PTO-1449 filed 11/30/04, reference CD). However, said enzyme does not posses the dual activity exhibited by the enzymes of the instant invention.

The specification does not support the broad scope of the claims which encompass heparin synthases with the dual activity having an amino acid sequence with no known identity to SEQ ID NOs: 2, 13 or 15 or having at least 70% identity to SEQ ID NOs: 13 or 15 or encoded by a DNA that hybridizes to SEQ ID NOs: 12 or 14 under hybridization conditions recited in clause "(D)" of claims 8 and 19, because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting a heparin synthase activity; (B) the general tolerance of heparin synthases to modification and extent of such tolerance, see the discussion above regard ding the Townsend et al reference; (C) a rational and predictable scheme for modifying any residues in heparin synthases with an expectation of obtaining the

desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Furthermore, with regard to claims 19-23, while the specification enables for a method for elongating the functional acceptor using the enzymes of the instant invention in the presence of a divalent ion, it does not enable said method in the absence of the divalent ion.

Without sufficient guidance, beyond that provided, obtaining a heparin synthase having an amino acid sequence with no known identity to SEQ ID NOs: 2, 13 or 15 or having at least 70% identity to SEQ ID NOs: 13 or 15 or encoded by a DNA that hybridizes to SEQ ID NOs: 12 or 14 under hybridization conditions recited in clause "(D)" of claims 8 and 19 as well as for a method for elongating the acceptor without a divalent ion is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 and claim 19, with dependent claims 20-23, recite "a complement" of a nucleotide sequence. Article "a" implies that the term encompasses sequences that may be not 100% complementary and/or complementary not to the full length nucleotide sequence, rendering the metes and bounds of the claims unascertainable.

Claim 19 recites "soluble heparin/heparosan synthase is selected from the group consisting of: (A) a soluble heparin synthase ..." (emphasis added). The use of different names renders the claim confusing.

Further, claim 19 recites "UDP-sugar analogs". The metes and bounds of the term "analogs" are not defined in the specification, rendering the claim unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8 and 19-23 are rejected under 35 U.S.C. 102(b) as being anticipated by DeAngelis et al.

DeAngelis et al (JBC, March 1, 2002, Vol. 277, pages 7209-7213, form PTO-1449 filed 11/30/04, reference CG) teach heparosan synthases from *Pasteurella multocida* and a nucleic acids encoding thereof (GenBank accessions AF425591 and AF439804, page 7209). AF 425591 is 100% identical to SEQ ID NO: 1 and it encodes

the amino acid sequence that is 100% identical to SEQ ID NO:2 of the instant invention. AF425591 encodes the sequence residues 46-617 differ from residues 2-573 of SEQ ID NO:13 by a single substitution (99.7% identical). AF439804 encodes the sequence that differs from SEQ ID NO:2 by a single substitution (99.8% identical). SEQ ID NO:13 is 99.8% identical to the amino acid sequence encoded by AF439804 with residues 2-573 of SEQ ID NO:13 being 100% identical to residues 46-617 of the DeAngelis sequence. Therefore, DeAngelis teach heparin synthases having at least 70% identical to SEQ ID NOs: 2, 13 and 15 that are encoded by a DNA that hybridizes to SEQ ID NOs: under low, medium and high stringency conditions or a DNA comprising a fragment of SEQ ID NOs: 1, 3, 12 or 14.

DeAngelis et al teach a method for producing a heparin polymer, i.e. the method of claim 8 (pages 7210-7211) and a method for producing a polymer by elongating the functional acceptor, i.e., the method of claims 19-23 (page 7211, Table 1, Figure 2). They teach that both methods must be carried out in the presence of the divalent ions (page 7211, 1st column).

NOTE: SEQ ID NOs: 1 and 2 are disclosed in provisional application 60/303,691 filed July 6, 2001, to which the parent application 10/142,143 filed May 8, 2002 claims priority, SEQ ID NO:3 is disclosed only in 10/142,143. However, SEQ ID NOs: 12-15 are disclosed neither in 10/142,143 nor in 60/458,939 filed March 31, 2003. Therefore, the effective filing date for the purposes of the prior art with regard to SEQ ID NOs: 12-15, is the filing date of 10/814,752, i.e. March 31, 2004.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

December 20, 2007